

Appl. No.: 10/567,899
Amdt. Dated 04/04/2008
Reply to Office action of December 4, 2007

REMARKS/ARGUMENTS

Claims 1, 2, 6, 8-16, and 19-32 have been rejected. Claims 1, 23, and 24 have been amended, and claim 8 has been cancelled to remove the term “prevention.” Applicants expressly reserve the right to file continuing applications or take other such appropriate measures to seek protection for the inventions encompassed by the cancelled subject matter.

These claim amendments were not presented earlier as Applicants earnestly believe that the previously presented claims recited patentable subject matter. The Examiner is respectfully requested to enter these claim amendments to further prosecution or to place the application in better condition for appeal.

Claims 1, 2, 6, 8-16, and 19-32 are pending in the application. Reconsideration of the claims is respectfully requested in view of the following remarks. The Examiner’s comments in the Office Action dated December 4, 2007 are addressed below in the order set forth therein.

The Rejection of the Claims Under 35 U.S.C. §102(a) Should Be Withdrawn

Claims 1, 2, 8, 23, and 24 have been rejected under 35 U.S.C. §102(a) as being anticipated by Batista *et al.* (WO 02/096443 A1). This rejection is traversed for the reasons provided below.

The Examiner states that this rejection has been maintained on the basis that the claims recite “prevention” of ventricular fibrillation. Although Applicants disagree with the Examiner’s assertion that use of the term “prevention” renders these claims anticipated by Batista *et al.*, for the purpose of expediting prosecution Applicants have amended the claims as described above to remove the term “prevention.” Accordingly, Applicants assert that this rejection has been rendered moot and request that it be withdrawn.

The Rejections of the Claims Under 35 U.S.C. § 103(a) Should Be Withdrawn

The Examiner has rejected claims 1, 2, 6, 8-10, 23, 24, and 26-32 for allegedly being obvious in view of the combination of Andre *et al.* (WO200296441) and Sander *et al.* (US 6,335,039). This rejection is traversed for the reasons provided below. References cited herein

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that are not already of record have been cited in an Information Disclosure Statement filed concurrently herewith.

One of the necessary elements for establishing a *prima facie* case of obviousness is that the prior art references must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). The rejected claims are drawn to the treatment or prevention of ventricular fibrillation. The Examiner has acknowledged that neither Andre *et al.* nor Sander *et al.* explicitly teach the treatment of ventricular fibrillation. Both Andre *et al.* and Sander *et al.* teach methods for producing vasodilation using *Trichilia* and other plants. However, as Applicants argued in their last response, there is no teaching or suggestion in Andre *et al.* or Sander *et al.* of the treatment of ventricular fibrillation.

In response to the above argument, the Examiner stated that “since the claims rejected under this 103 recite ‘prevention’ of ventricular fibrillation, it does not require that the patient is suffered [sic] with ventricular fibrillation, and the claims are broad enough to read on anyone who is being administered with [sic] the claimed extracts, thus the 103 rejection stands” (page 7 of the Office Action dated December 4, 2007). As described above, Applicants have amended the claims to remove the term “prevention”. Accordingly, Applicants assert that this rejection has been rendered moot and request that it be withdrawn.

The Examiner has also rejected claims 1, 2, 6, 8-10, 15, 16, and 23-32 for allegedly being obvious in view of the combination of Andre *et al.* and Sander *et al.*, further in view of Kowey *et al.* (*Cardiovascular Res.* 17:106-112 (1982)). This rejection is traversed for the reasons provided below.

Although the U.S. Supreme Court recently declined to permit a “rigid” application of the teaching-suggestion-motivation to combine (TSM) test to obviousness determinations, the Court did hold that the presence or absence of a teaching, suggestion, or motivation to combine the cited references provides a “helpful insight” regarding the obviousness of an invention. *KSR Int'l Co. v. Teleflex, Inc.*, 82 USPQ2d 1385 (U.S. 2007). The Supreme Court went on to acknowledge the importance of identifying “a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in way the claimed invention does” in

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an obviousness determination. *Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd.*, 83 USPQ2d 1169 (Fed. Cir. 2007; citing *KSR Int'l Co. v. Teleflex, Inc.*; emphasis added). In the instant case, Applicants submit that one of skill in the art would not have had any reason to combine the references cited by the Examiner to arrive at the present claims.

As a reason for combining the cited references, the Examiner states that Kowey *et al.* allegedly teaches that ventricular fibrillation can be abolished by pretreatment with vasodilators, and that both Andre *et al.* and Sander *et al.* teach methods for producing vasodilation using *Trichilia* and other plants. In response to Applicants' previous arguments, the Examiner states that "Andre et al., Sander et al. teach the four claimed plant extracts [and] choosing from a finite number of predictable solutions would have been obvious because a person of ordinary skill has good reason to pursue the known options with his or her technical grasps [sic]" (page 10 of the Office Action dated December 4, 2007). Applicants disagree.

In *Ortho-McNeil Pharmaceutical Inc. v. Mylan Laboratories Inc.*, slip op. 2007-1223 (Fed. Cir. Mar. 31, 2008), the Federal Circuit held that the FBPase inhibitor topiramate and its use as an anticonvulsant were not obvious. In its decision, the Federal Circuit rejected the argument that because FBPase inhibitors were known to be useful to treat diabetes, one of skill in the art would have had a reason to design such inhibitors because of "a design need or market pressure to solve a problem" and because of "a finite number of identified, predictable solutions." *Id.*, slip op. at 9. In particular, the court found that there was significant evidence to show that the identification of topiramate "[did] not present a finite (and small in the context of the art) number of options easily traversed to show obviousness." *Id.* The court pointed to the unpredictability of the art and the need to test topiramate to determine whether it demonstrated anticonvulsant properties, and rejected an approach to obviousness that "simply retraced the path of the inventor with hindsight, discounted the number and complexity of the alternatives, and concluded that the invention of topiramate was obvious." *Id.* at 10.

In the present case, Applicants submit that the discovery that the claimed plant extracts were useful in the treatment of ventricular fibrillation did not represent a selection "from a finite number of predictable solutions" as the Examiner argues, but instead reflects the identification of the claimed plant extracts as having efficacy for a new use (ventricular fibrillation) in spite of the number,

complexity, and unpredictability of the alternatives. As Applicants have previously asserted, the term “vasodilator” encompasses a wide range of structurally distinct compounds that may impact vasodilation through any number of distinct physiological mechanisms. Even if a given compound were identified as belonging to this widely divergent class of functionally defined compounds, one of skill in the art would not have a reasonable expectation that such a compound would be successful in the treatment of ventricular fibrillation. This unpredictability is acknowledged by Kowey *et al.*, who state that although they observed protective effects of prostacyclin, prostaglandin E₁, and nitroglycerin on vulnerability to ventricular fibrillation, “[i]t remains to be determined whether other vasodilator drugs possess a similar potential for protection against malignant arrhythmia” (see Conclusion on page 111 of Kowey *et al.*). In fact, studies of patients with congestive heart failure to whom vasodilators have been administered have failed to show any reduction in ventricular fibrillation (although global mortality was reduced; American College of Cardiology/American Heart Association 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult (2005) *Circulation* 112(12):e154-e235). Accordingly, at the time of the invention, one of skill in the art would not have had a reasonable expectation of success in treating ventricular fibrillation using the claimed plant extracts.

Applicants also note that experimental evidence suggests that the observed effect of the claimed plant extracts on ventricular fibrillation does not appear to be due to vasodilating effects, but is instead due to clear and evident electrophysiological actions on the heart (see Pontieri *et al.* (2007) *J. Electrocardiology* 40(6):534.e1-534.e8). Pontieri *et al.* demonstrated that *Catuama* and *Trichilia Catigua* prolonged conduction time, *Catuama* prolonged phase 2 of the monophasic action potential (MAP), and *Ptychopetalum olacoides* prolonged phase 3 of the MAP. These results suggest specific actions of the claimed plant extracts on the membrane channels of the heart, and consequently on heart electrophysiology, which is absolutely different from vasodilating effects.

In summary, because one of skill in the art would not have had a reasonable expectation of success in treating ventricular fibrillation using the claimed plant extracts, a *prima facie* case

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of obviousness has not been established. Applicants therefore request that this rejection be withdrawn.

CONCLUSION

In view of the aforementioned amendments and remarks, Applicants respectfully submit that the rejections of the claims under 35 U.S.C. §§102(a) and 103(a) are overcome.

Accordingly, Applicants submit that this application is now in condition for allowance. Early notice to this effect is solicited.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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